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| EXAMINER | |
|---|---|
| WESSENDORF, TERESA D | |
| ART UNIT | PAPER NUMBER |
| 1636 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/880,688 | POUSTKA ET AL. | |
| | Examiner | Art Unit | |
| | TERESA WESSENDORF | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10/2911 and 5/12/11*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

5)☒ Claim(s) *75,78-82,84 and 86-100* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *75, 78-82, 84 and 86-100* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

***Status of Claims***

Claim 75, 78-82, 84 and 86-100 are pending in the instant application and under examination.

Claims 1-74, 76-77, 83(is missing from the instant claims and assumed to be cancelled) and 85 have been cancelled.

***Priority***

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Germany on 12/14/1998 and 7/30/1999. It is noted, however, that applicant has not filed a certified copy of the GERMANY 198 57 529.7 and GERMANY 199 35 553.3 applications as required by 35 U.S.C. 119(b). Therefore, the filing date of the instant application is deemed to the filing date of the PCT/DE99/03982 application of **December 14, 1999.**

Applicants' claim for foreign priority is not perfected because the foreign priority document(English translation filed on 9/20/10) fails to provide adequate support for the currently claimed invention under 35 U.S.C. 112, first paragraph (e.g., see MPEP § 706.02(b), "The filing date of the [foreign] priority document is not perfected unless ... the examiner has

established that the priority document satisfies the enablement and description requirements of 35 U.S.C. 112, first paragraph"; see also In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989) (generic and subgeneric claims in the U.S. application were not entitled to the benefit of foreign priority where the foreign application disclosed only two of the species encompassed by the broad generic claim and the subgeneric Markush claim that encompassed 21 compounds).

***Withdrawn Objections/Rejections***

In view of the amendments to the claim numberings, the objection to the claims is withdrawn. Also, in view of the amendments to the claims and applicants' arguments the rejections under 35 USC 112, 2nd paragraph and 35 USC 102 over Blanchard are withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Claim Rejections - 35 USC § 112***

Claims 75, 78-82, 84 and 86-100 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the

written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record as reiterated below i.e., only for the maintained rejections.

***New Matter Rejection***

The following amendments in claim 75 do not find support in the as-filed specification:

1). “Embedding of monomers within a solvent”,

***Response to Arguments***

1) Applicants argue that the "embedding of the monomers within a solvent" is clearly from the original claims. Applicant is not required to state everything verbatim from the specification in the claims. Other paragraphs in the application refer to "dissolving .... immobilizing", "incorporated" "contained" are used synonymously. Claim 15 of the initial disclosure uses the term "embedding into a matrix". It is clear from the disclosure including the claims initially filed that the term is not new matter. The embedding process is clearly outlined in the specification in [0125]. Others are found in

[0024], [0029], [0037], [0049], [0055], [0057], [0093], [0095], [0123]. Issue is taken with the Examiner's repeated objection to the same wording, especially that the Examiner questions how monomers can be embedded in a solid solvent. Applicant has provided repeatedly references to "matrix" including that the matrix is shown in Figure 25 and referred to in the description to Figure 25 in the specification.

In reply, as applicants stated above original claim 15 recites "embedding into a **matrix**" which include other components such as magnetic particles as disclosed in the specification and is a broader composition than only a solvent, as presently claim.

Paragraph [0125] relied upon above, discloses “various phosphoramidites provided with protective groups together with magnetite particles are dissolved in diphenyl formamide/acetonitrile at 25 °C, shock-frozen and the soluble constituent sublimed at low temperatures. They are then finely ground so as to produce particles as uniform as possible, approx. 1- 200 um in diameter, especially 2-40 um in diameter. These particles are loaded into toner cassettes and printed on paper”.

This paragraph does not provide support for the now claim "embedding monomers within a solvent that is in solid state of aggregation."

Paragraph [024] also relied upon above, discloses that "the diffusion of the monomers is significantly limited and said first solvent used is prevented from vaporizing partly or completely during the application of the monomers or during the linking reaction.

The claims do not recite for first and second solvents, but embedding of monomers within a solvent (not solvents).

Furthermore, none of the other above cited sections as provided below provides support for the presently claim embedding within a solvent the monomers:

Paragraph [029] discloses "the particles and/or the immobilized substance can be melted or dissolved by a second substance or brought into a gel-like state".

Paragraph [037] discloses "in an additional method said monomers for combinatorial synthesis are incorporated in 0.2 um to 200 um, preferably 2 um to 40 um monomer-toner particles which at room temperature take on the solid state of aggregation. The © term room temperature describes a temperature range between -10 °C and 80 °C, but preferably between 0°C and 40 °C. Another characteristic of these particles is that with

said first solvent they contain an inert constituent relative to the linking reaction, whose state of aggregation can be modified as described above. Preferably said particles also contain magnetic constituents or bind to particles which contain magnetic constituents. In FIG. 7 such a monomer toner particle is compared schematically with a normal chromophore toner particle.

As stated above the claims do not recite for first and second solvents or a magnetic constituents or monomer-toner particles. None of the remaining paragraphs recite embedding amino acid monomers within a (single) **solvent.**

While applicants are permitted to be his own lexicographer however, it carries with it the connotation that applicants will use terms consistently throughout his patent. Porter v. Farmers Supply Services Inc., 228 USPQ 4. MPEP 2111.01[R5] IV. Thus, the used of different terminologies in the specification and claims provide for confusion and ambiguity.

4). The entire claim 87.

***Response to Arguments***

4) Applicant is at a loss to understand the new matter rejection since the wording the Examiner considers is not mentioned. The Examiner should specify the terms the Examiner

deems new matter in claim 87 and discuss them, so that applicant can respond.

In reply, the rejection above clearly indicates the entire steps of newly added claim 87(amended on 4/13/09) is not found in the original specification and not in the use of each or certain terms in the claim as argued.

Applicant notes that the instant application was handled by a number of Examiner's and has been pending for more than 9 years. It is not understood why at this stage why applicant has to explain again every term used in the claims.

In reply, it is noted that throughout the prosecution of the case, the claims have been amended each time after issuance of the Office action. At some instances non-compliant letters were mailed on 9/9/04, 11/15/04, 3/15/05, 4/28/05, 3/10/06 and 7/19/06) due to the claim amendments.

As stated above the issue in claim 87 are not the terms use in the claim. Rather, the entire steps in claim 87 (which is added or amended on 4/13/09) i.e., in its entirety is not in the original disclsoure.

***Written Description Rejection***

Claims 75, 78-82, 84 and 86-100, as amended and newly added, are rejected under 35 U.S.C. 112, first paragraph, as

failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., Moba, B.V. v.Diamond Automation, Inc., 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed.Cir. 2003); Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116.

The specification fails to describe the method steps of embedding at least two different amino acid monomers or oligonucleotide monomers at a temperature of less than 90° C within a solvent that is in a solid state of aggregation, thereby forming monomer-immobilizing transport units. It is not apparent from the as-filed disclosure how the different monomers are embedded within a solvent that is in a solid state of aggregation. Furthermore, there is no detail description of any solvent(s) that is in a solid state of aggregation at said temperature. The specification merely provides the definition at e.g., page 1, paragraph [0009] that the term "solid state of aggregation" also includes undercooled liquids. The definition

is confusing in that it failed not only to define the kind/type of solvent in the solid state of aggregation but also what are the solvents included or precluded in the undercooled liquids. The specification describes the solvent in terms of the single solvent diphenylformamide, e.g., page 4, paragraph [0051]. There is no description as to how the single solvent is embedded with the monomers at the given temperature. Furthermore, it does not describe how this single solvent represents the numerous solvents covered by the huge genus undercooled solvents. The general statements in the specification are therefore not a detail description of the invention.

A "written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials". University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993).

***Response to Arguments***

The Examiner is directed to [0123] and [0125] for the dissolving of the monomers into the solvent at the specified

temperatures. Once the solvent is solid again, the monomers are deemed to be embedded.

In reply, [0123] recites "various amino acids provided with protective groups, especially fMoc protective groups, especially also the corresponding anhydrides together with magnetite particles are dissolved in diphenyl formamide at 75 °C, shock-frozen and finely ground, so as to produce particles as uniform as possible, approx. 1-200 pm in diameter, especially 5-40 pm in diameter. These particles are loaded into toner cassettes and printed on paper. FIG. 19 compares the print quality of a normal toner with various amino acid toners." [0125] recites various phosphoramidites provided with protective groups together with magnetite particles are dissolved in diphenyl formamide/acetonitrile at 25°C, shock-frozen and the soluble constituent sublimed at low temperatures. They are then finely ground so as to produce particles as uniform as possible, approx. 1-200 um in diameter, especially 2-40 pm in diameter. These particles are loaded into toner cassettes and printed on paper".

In reply, none of the claims recite for the steps of dissolving of the monomers in dipenylformamide with magnetite particles as the solvent as recited in each of the above paragraphs. Rather only embedding a monomer into a sinlge

solvent for claim 75, for example. The claim process steps comprise only the embedding of monomers into a solvent at less than 90°C.

It is well settled that though understanding the claim language may be aided by explanations contained in the written description, it is important not to import into a claim limitations that are not part of the claim. For example, a particular embodiment appearing in the written description may not be read into a claim when the claim language is broader than the embodiment. Superguide Corp. v. DirecTV Enterprises, Inc., 358 F.3d 870, 875, 69 USPQ2d 1865, 1868 (Fed. Cir. 2004). MPEP 2111.01[R5](II).

The Examiner states that it is not apparent from the disclosure how the different monomers are embedded within the solvent. Applicant points to [023], [057] to [059] and [0123] to [0127]. The characteristics of the solvent are given in [023]. The printing method is stated in [093] and the operation of the laser printer in [096]. The description of the dissolution of the monomers in the solvent and the preparation of toner particles is amply described in [095], [0123] and [0125] in which various methods are described how the toner particles are made. The Examiner is directed to the fact that the invention

does not rest in the solvent per se but in the fact that a phase shift can be accomplished by creating these transport units with various solvents that have the stated criteria in order to immobilize and then mobilize the monomers to diffuse them on the support for the combinatorial libraries. In summary, applicant contends that the description contains everything to practice the invention. In view of the foregoing, it is believed that all terms in the claims and all claim steps are referred to and explained in the specification. Withdrawal of the rejection of claims 56-60, 66-67, 69-71, 75, 78-84, 86 and 87 is thus respectfully requested.

In reply, as a preliminary matter the claims under rejections are not 56-60, 66-67, 69-71, 75, 78-84, 86 and 87 but claims 75, 78-82, 84 and 86-100 as stated above. However, instead of issuing a one month non-compliant for the amendments/ responses and for compact prosecution, the one month non-compliant amendments/responses are waived.

The description throughout the specification does not relate only to a single solvent or to a solvent per as claimed. Rather, the description in the specification describes solvent in the presence of magnetic constituents such that the solvent can be in the state of aggregation, as claimed. The description in the specification is not an issue of whether all the terms

are in the original specification. Rather, the numerous different kinds of solvent in state of aggregation that dissolves a monomer for mobilization onto a support.

***New Rejections Necessitated by Claim Amendments***

***Claim Rejections - 35 USC § 112***

Claim 90 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 90 recites the limitation "the monomers bind to particles that include magnetic constituents". There is insufficient antecedent basis for this limitation in the base claim 75 which does not recite for said binding of the monomers. It is vague and indefinite as to which step in claim 87 the monomer binding to the particles take place. Furthermore, it is indefinite as to what comprises “constituents” of the magnet.

***Claim Rejections - 35 USC § 103***

Claims 75, 78-82, 84 and 86-100, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Blanchard (USP 6028189) (as evident by The Condensed Chemical Dictionary) in view of Zebala (USP 6951682) and Anderson(USP 7179638) for

reasons of record as repeated below and modified to address the new claim amendments and applicants' arguments.

For claims 75, 80-82, 84, 86, 91-93, 96, 97, 98 and 100; Blanchard discloses throughout the patent at e.g., col. 2, line 46 up to col. 4, line 30, a method of oligonucleotide synthesis comprising chemically coupling a first nucleotide monomer to a second nucleotide monomer in a high surface tension solvent (i.e., embedding step with a solvent in state of aggregation, as claimed in e.g., claim 75). Blanchard discloses the step-by-step synthesis at e.g., col. 3, lines 19-50 which comprises: (a) applying at least a first reagent dissolved in propylene carbonate to said surface, wherein said substrate is chemically prepared to react with said first reagent to covalently attached said reagent to said substrate; (b) applying at least one either the first reagent or a second reagent dissolved in propylene carbonate to said surface wherein said substrate is chemically prepared to react with said reagent to covalently attach said reagent to said substrate; (c) optionally repeating step (b) at least one time using the same or different reagents dissolved in propylene carbonate wherein each of said reagents covalently attaches to said substrate to form covalently attached compounds; (d) washing said substrate to remove unattached reagents; (e) modifying said attached reagents; and (f)

repeating steps (a) through (e) at least once with the same or different reagents dissolved in propylene carbonate at various loci on the substrate. Using the above method, a plurality(library as claimed) of different chemical compounds within the array can be simultaneously synthesized.

Blanchard discloses at e.g., col. 3, lines 2-5, an automated assembly of the oligonucleotides into the array using an ink-jet pump apparatus to deliver the first and second nucleotide monomers to a specified position on a solid support.Blanchard further discloses at e.g., col. 8, lines 15-18, application of reagent to the wells using e.g., an ink-jet printer, a laser printer with a soluble toner, evaporation or by a photolithographic process.

For claims 91-96, Blanchard discloses the propylene carbonate, (reads on the claim solvent in solid state of aggregation) which is supercooled (undercooled) liquid at a temperature of -49oC (please see the Condensed Chemical Dictionary).

For claim 98, Blanchard discloses at e.g., col. 6, lines 5-8, “to extend the chain, one of the two terminal protecting groups must be removed selectively to generate a free hydroxyl function to which a new partially protected unit can be joined.”

{Noteworthy is applicants' claim 98 that claims "detaching protective groups by **standard methods**"). (Emphasis ours.)

For claim 99, Blanchard discloses at e.g., col. 5, line 12-18, the substrate as paper or polystyrene.

For claim 100, Blanchard discloses at e.g., Figure 2 a transient voltage applied to the piezoelectric actuator.

The claim temperature of the solvent in solid state of aggregation is a property considered inherent to the compound of Blanchard i.e., propylene carbonate which is an undercooled liquid at -42oC.

Blanchard does not expressly disclose a matrix by which the nucleic acid is embedded including the solvent at a temperature of less than 90oC as in claim 87 or the temperature in a range of -10oC and 80oC as in claim 78 or 0oc and 40oC as in claim 79.

However, Zebala discloses at e.g., col. 72, lines 1-20; polymeric films contain one or more receptors and/or indicator compounds in a polymer matrix comprising, for example, polyvinyl alcohol or any other such polymer compatible with detecting binding of particular ligands and receptors. In some embodiments, the films will be photopatternable, and will

typically swell when hydrated forming a polymeric gel. After either chemical or photolytic release from the support, ligands will diffuse into the surrounding gel matrix. If a particular group of ligands specifically binds the receptors in the gel, then a zone of activity will be visible around that group. Determining the position of the element will reveal the reagent history, or more preferably, the composition of the ligand in a straightforward fashion.

Anderson discloses at e.g., col. 13, lines 35-50 that solidifying matrix holding the reagent(s) may be dissolvable, meltable, degradable, or reversible to further enhance interaction. Anderson further discloses at e.g., col. 36, lines 63 up to col. 37, line 6 porous particles (with many internal crevices), has a diameter of approximately 5 microns. Attached proteins are distributed over the internal surfaces as well as the exterior surface of the particle. By embedding the particles in a suitable medium, a sliceable solid matrix in which the antibody was immobilized and fairly uniformly distributed was created. By exploiting the 3-dimensional nature of the support, a slice containing such particles offers greater capacity (for antibody and thus for antigen binding).

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to embed the solvent aggregating monomer in a matrix in the method of Blanchard as taught by Zebala and Anderson. One would have a reasonable expectation of success since different components/substances have been deposited into an array by a matrix which contains the compound or reagent of interest. A compound/substance in a matrix, makes the compound e.g., antibody fairly uniformly distributed on the array. A support containing a particle in a matrix offers greater capacity for compound interaction as taught by Anderson. Zebala teaches the conventionality of using a matrix containing a substance in a solvent. Blanchard likewise suggests that matrix in an array has been used in the art citing e.g., Brennan. One having ordinary skill in the art would have a reasonable expectation of success in using a matrix to deposit in an array a compound therein as successfully shown by the different cited prior art above. A compound embedded in a matrix provides for a uniform distribution of said compound when applied to a surface.

The claim temperature of the solvent is a result effective variable well within one of ordinary skill in the art to determine. Said temperature, if not an inherent property of the

solvent at hand, would be within one of ordinary skill in the art to determine.

The claim method of synthesizing monomers by depositing a solvent containing the compound being synthesized on an array using either an ink-jet or laser printer is well-practiced in the art at the time of the invention.

> If a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. When considering obviousness of a combination of known elements, the operative question is thus "whether the improvement is more than the predictable use of prior art elements according to their established functions." KSR International Co. v. Teleflex Inc., 550 USPQ2d 1385 (2007).

***Response to Arguments***

At the outset it is noted that the Anderson reference has been overcome as prior art since applicant has perfected its priority and the priority date of applicant antedates the Anderson reference.

In reply, Anderson is still a proper reference. Please see the priority grant above.

Applicants argue that Blanchard uses a high surface tension solvent for the combinatorial synthesis of oligonucleotide array. The high surface tension solvent is exemplified in Fig. la. The reason for using high surface tension solvent is stated as "very small reagent droplets can be localized and separated from each other" "and act as miniature reaction vessels for oligonucleotide synthesis". Surface tension is the property of a liquid to resist an external force. Blanchard is thus in line with the conventional combinatorial synthesis methods, except the ability to localizing and separating small reagent droplets. The Blanchard method is entirely distinguishable from the above method. Blanchard does not teach that the (high-tension) solvent is in a solid state or a monomer could be embedded into the solvent in a solid state of aggregation. Blanchard does not teach that a high-tension solvent could be used as an undercooled liquid, nor does Blanchard teach to work below -49°C, where propylene carbonate is an undercooled liquid as claimed by the Examiner. Blanchard merely dissolves the monomers in propylene carbonate under standard conditions "by substituting a known coupling buffer or solvent with a high surface tension solvent", col. 5, lines 47-57. Blanchard does not embed monomers in a solid state of aggregation, as suggested by the Examiner. Blanchard does not teach the use of a laser

printer for delivering monomers to the surface, as implied by the examiner, Blanchard instead uses "microfabricated ink-jet pumps or nozzles similar to those used in ink-jet printers" co1.8, lines 24-38 and pumps that deliver 100pL droplets for oligonucleotide synthesis in two dimensional arrays, col. 8, lines 53-67.

In reply, Blanchard's disclosure of below 49°C is interpreted at room temperature read in light of the disclosure teachings at [037]. "In an additional method said monomers for combinatorial synthesis are incorporated in 0.2 um to 200 um, preferably 2 um to 40 um monomer-toner particles which at room temperature take on the solid state of aggregation. The term room temperature describes a temperature range between -10°C and 80 °C, but preferably between 0 °C and 40".

As recognized by applicants above, "Blanchard dissolves the monomers in propylene carbonate under **standard conditions**" which would include the room temperature, 25°C, since Blanchard teaches a temperature less than 49°C. See also applicants' statement above that "... the application refer to "dissolving .... immobilizing", "incorporated" "contained" are used synonymously". Furthermore, whether the solvent use by Blanchard has a property of high surface tension is immaterial inasmuch as

the solvent dissolves the monomers and successfully applied the monomers to the surface at defined locations("localizing and separating small reagent droplets", as applicants stated above).

Applicants argue that both Blanchard and Zebala do not teach the laser printer method in the manner as claimed and the Anderson reference cannot add anything to the combination of Blanchard and Zebala since it is no longer valid as a reference. With respect to the Examiner's statement that in col. 8, lines 15-18 Blanchard discloses application of a laser printer with a soluble toner, evaporation or by a photolithographic process, applicant responds that a laser printer is merely and explicitly used to pre-structure a solid support for later use in the combinatorial synthesis NOT for addressing monomers to the surface for combinatorial synthesis.

In reply, Anderson is still a valid reference as discussed above. Blanchard uses the laser printer with a soluble toner, col. 8, lines 15-18, to pre-structure a solid support for combinatorial synthesis, which suffices the findings of obviousness. It would be within the ordinary skill in the art to use the laser in combinatorial synthesis given that the prior art already successfully use said laser printing in the pre-structure solid support for combinatorial synthesis has been

made. The same principle of immobilization of monomers using soluble toner would obviously apply in immobilizing monomers for combinatorial synthesis using said solid support. If a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. When considering obviousness of a combination of known elements, the operative question is thus "whether the improvement is more than the predictable use of prior art elements according to their established functions." KSR International Co. v. Teleflex Inc., 550 USPQ2d 1385 (2007). Similarly, herein the technique of using laser printing to immobilize monomers in soluble toner on solid support is taught by Blanchard.

Applicants argue that the Examiner admits that Blanchard does not disclose a matrix by which the nucleic acid is embedded including the solvent at a temperature of less than 90°C etc. (see page 18 OA). Therefore the Examiner uses the Zebala reference as supplying those elements. Zebala's invention is obviously in a support with an especially large surface area that has nothing to do with monomers that are embedded in particles. The Examiner states that Blanchard discloses

application of a reagent to the wells using an inkjet printer, laser printer with soluble toner, evaporation or by a photolithographic process. However, similar to Zebala, a laser printer is merely and explicitly used to pre-structure a solid support NOT for addressing the monomers to the surface for combinatorial synthesis. Like Blanchard, Zebala does not use laser printing. Zebala refers to a lithographic methods. Blanchard refers to an ink jet method. All lithographic methods have severe drawbacks as also outlined in the description. In all lithographic methods a surface of the substrate is patterned into two kinds of areas, namely areas with protecting groups removed to allow for a chemical reaction and areas where the protecting groups are not removed thus hindering chemical reaction. Zebala is not directed to positioning at different times a pattern of different immobilized peptide or nucleic acid monomers in the form of transport units at a solid state of aggregation to a support, which transport units differ from each other by the monomers immobilized within; wherein the immobilized peptide or nucleic acid monomers are temporarily blocking a coupling reaction of the monomers to the support by the reversibly immobilized monomers; inducing a change in the transport units form the solid state of aggregation to a liquid state of aggregation, thereby permitting a free diffusion of the

monomers; then carrying out a coupling reaction to couple at least two different of the monomers to the support at the same time in one single combinatorial synthesis.

In reply, Zebala is not employed for the purpose as argued. Rather for its teachings of a matrix rather than simply a solvent as taught by Blanchard(as matrix is implicitly taught by Blanchard). It is Blanchard that teaches all the argued claim limitations above. Thus the combined teachings of the prior art would lead one having ordinary skill in the art to the claim method. Applicants cannot show non-obviousness by attacking the references individually where the rejection is based on a combination of references. In re Young, 159 USPQ 725 (CCPA 1968).

No claim is allowed.

***Allowable Subject Matter***

As suggested in the previous Office action and based on most of applicants' arguments above, a claim to the process steps disclosed in the specificioatn at e.g., para. [0123]-[125] would be allowable as the prior art does not teach these process steps.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the

organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/
Primary Examiner, Art Unit 1639